On page 1, directly below the heading METASTASIS INDUCING DNA's, please insert the following headings:

—Background Of The Invention—

1) —Field Of The Invention—

On page 1, before the paragraph beginning "Most cancers are thought to be due . . .", insert the following heading:

2) —Description Of Related Art—

On page 2, before the paragraph beginning "It is one object of the present invention to", insert the following heading:

3) —Summary Of The Invention—

On page 4, before the paragraph beginning "In one embodiment, fragments of human DNA from", insert the following heading:

4) —Detailed Description Of The Invention—

On page 5, please replace the paragraph at the bottom of the page beginning "To aid the rescue of metastasis-inducing human" with the following paragraph:

5) To aid the rescue of metastasis-inducing human DNA sequences from the rat transformant cell lines, all the HindIII-fragmented DNA's from one such metastatic transformant, R37-Ca2-LT1 (Table 1) were tagged at both ends with double-stranded synthetic oligonucleotides that provide restriction enzyme and unique PCR primer sites. (SEQ. ID. Nos: 7 and 8.) These are shown in Fig. 1 The tagged DNA fragments include 4 restriction sites: *Sfi*I and *Not*I, a defective *Hind*III site at the 3' end for linking to the *Hind*III sites at the ends of the human DNA fragments, thereby destroying it, and an internal *Hind*III site located near to the 5' end, which when cut after ligation generated new fragments with *Hind*III ends. The fragments were transfected into the parental Rama 37 cells, and after transfer of the cells to the mammary glands of syngeneic rats, metastatic cell lines were isolated from the resultant rat lung metastases. The tagged, fragmented DNA incorporated into the metastatic transfacted Rama 37 cell lines was directly amplified between the tags by PCR and yielded bands at about

1300 to 1500 bp that were responsible for the metastasizing ability of the transfected cells. These results are shown in Fig. 2 which shows the DNA fragments produced by PCR of metastatic transformants. Two new cell lines, established from the culture of lung metastases of R37-Ca2-HT (tagged, metastatic DNA transformant) and R37-Ca2-H (untagged, metastatic DNA transformant) (see Table 1) in rats were termed HTLu and Hlu, respectively. They were run against the tagged benign transformant cell line R37-B-HT and the tagged metastatic transformant R37-Ca2HT. Cellular DNA was amplified by PCR using a short oligonucleotide primer of 22 bp from positions 3-24 of the tag sequence as shown in Fig. 1. Compared with the control DNA's from Hlu and B-HT cells, two extra bands, F1 and F2, of about 1300 bp and 1500 bp respectively, were specifically amplified from genomic DNA of the Ca2-HT and HTLu cells when PCRed DNA samples were run on 0.8% agarose gels containing ethidium bromide and photographed in U.V. light. The fluorescent bands of DNA are shown in negative imaging for clarity. Cloning of these pooled DNA's yielded six independent fragments and the results are illustrated in Fig. 3. Fig. 3 shows pBluescript clones of metastatic DNA fragments F1 plus F2. The two broad PCR DNA fragments F1 and F2 were excised from the gel in Fig. 2, combined, and cloned directly using the AT procedure into a suitably modified pBluescript vector and the clones of recombinant vectors were cut with *Hind*III to excise the cloned fragments. These cut recombinant vectors were analysed on a 0.8% agarose gel containing ethidium bromide and photographed in U.V. light. The sequences of some clones eg. C10 and C9-DNA's were identical; the six independent sequences arose from clones numbered C2, C5, C6, C9, C12 and C20 and hence are referred to as C2-DNA, C5-DNA etc as shown in Fig. 3. The position of the vector (Vec) DNA and insert (Ins) DNA are indicated and a standard molecular weight ladder in kilobase pairs (kbp) is shown in lane M. Transfection of these cloned DNA fragments singly into the parental benign cell line confirmed that all fragments (C2, C5, C6, C9, C12 and C20-DNA's) produce metastases. These are shown in Table 2 which tabulates the incidence of tumours and metastases for Rama 37 cells transfected with cloned Met-DNA's. The superscript a - e indicate:

On page 9, please replace the paragraph at the bottom of the page beginning "Surprisingly, the sequences of these Met-DNA's" with the following paragraph:

Surprisingly, the sequences of these Met-DNA's (hereafter SEQ. ID. Nos.: 1-6), although human in origin, do not correspond to known genes and most do not include any known open reading frames. Furthermore none of these Met-DNA's are expressed as mRNAs in their transformants and hence are not dominantly-acting oncogenes. They therefore contain entirely novel short stretches of regulatory DNA capable of inducing metastasis.

On page 12, please replace the paragraph at the bottom of the page beginning "According to a third aspect of the present" with the following paragraph:

According to a third aspect of the present invention there are provided DNA consisting essentially of a regulatory DNA capable of inducing metastasis from SEQ. ID. NO. 1:

On page 13, please replace the paragraph in the middle of the page beginning "According to a fourth aspect of the present" with the following paragraph:

According to a fourth aspect of the present invention there are provided DNA consisting essentially of a regulatory DNA capable of inducing metastasis from SEQ. ID. No. 2:

On page 14, please replace the paragraph at the top of the page beginning "According to a fifth aspect of the present" with the following paragraph:

According to a fifth aspect of the present invention there are provided DNA consisting essentially of a regulatory DNA capable of inducing metastasis from SEQ. ID. NO. 3:

On page 14, please replace the paragraph in the middle of the page beginning "According to a sixth aspect of the present" with the following paragraph:

According to a sixth aspect of the present invention there are provided DNA consisting essentially of a regulatory DNA capabel of inducing metastasis from SEQ. ID. NO. 4: